

paragraph set forth below. (Appendix A, which is enclosed herewith, shows how the fourth paragraph on page 14 was amended to produce the amended paragraph set forth below. In Appendix A, the portions being added are underlined; and the portions being deleted are enclosed in brackets.)

Sequence: In order to comply the above conditions, the polypeptides object of the present invention must include in their sequence the following consensus sequence (SEQ ID NO:1):

$Z_{3-48} CZ_{9-13} C(Q,E,R,K) Z(Z_{\text{hydrophobic}}) (LIVM) Z_{15-39} CC(Z_{\text{hydrophilic}})$

$(Q,E,H) (L,V) Z_6 CZC Z_2 (L,I) Z_{13-56} G Z_{15-26} CZ(V,I,L,M) Z_{1-8} CZ_{1-12}$

(() Indicates 1 amino acid, being within the parenthesis the possible ones in order of preference. Z_n indicates n amino acids whichever they are. This sequence has CZ_nC domains (Tamaoki et al "Folding motifs induced and stabilized by distinct cystine frameworks" Protein engineering 11, 649-659 (1998)).

A3 "SECRETED"

Please replace the first paragraph on page 25 of the specification (see lines 1-21 on page 25) with the amended paragraph set forth below. (Appendix A, which is enclosed herewith, shows how the first paragraph on page 25 was amended to produce the amended paragraph set forth below. In Appendix A, the portions being added are underlined; and the portions being deleted are enclosed in brackets.)

A4
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is dimeric, as determined by polyacrylamide gel electrophoresis denaturing and reducing conditions (H Schagger, G von Jagow "Tricine-sodium dodecyl sulfate polyacrylamide gel electrophoresis for the separation of proteins in the range from 1 to 100 KDa" Anal. Biochem. 166,368-379 (1987)), the dimers being united by disulphur bridges as can be deduced from the need to use reducing conditions for the resolution by electrophoresis; it is resistant to trypsin (incubated for 24 hours at 37°C in 0.1 M Tris-HCl pH 8.5 in a polypeptide protease ratio 30:1), pepsine (incubated 24 hours at 37°C in 0.01 M HCl in a polypeptide protease ratio 25:1) and complies with the rest of the requirements described in the General Specifications of the Invention. Its sequence, determined by Edman degradation, is as follows :

Minor subunit: ESKGEREGSSSQ^QCRQEVQ^RKDLSSC^ERYLRQSSRR
(SEQ ID NO:2)

Major subunit:

QQQESQQLQ^QCCN^QVKQVRDECQ^ECAIKYIAEDQIQ^QQLHGEESERVAQRAGEIVS
SCGVRCMRQTR (SEQ ID NO:3)

(the amino acids specified in the consensus sequence are underlined)

Please replace the first paragraph on page 29 of the specification (see lines 1-11 on page 29) with the amended paragraph set forth below. (Appendix A, which is enclosed herewith, shows how the first paragraph on page 29 was amended to produce the amended paragraph set forth below. In Appendix A, the portions being added are underlined; and the portions being deleted are enclosed in brackets.)

hours at 37°C in 0.01M HCl in a polypeptide protease ratio 25:1) and complies with the rest of the requirements described in the General Specifications of the Invention. Its sequence, determined by Edman degradation is as follows :

Minor subunit: PSQQGCRGQIQEQNLRQCQEYIKQQVSGQGPRR (SEQ ID NO:4)

Major subunit:

QERSLRGCCDHLKQMSQCRCEGLRQAIEQQSQGQLQGDVFEAFRTAANLPSMCG
VSPTECRF (SEQ ID NO:5)

(the amino acids specified in the consensus sequence are underlined)

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